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EXAMINER	
BASKAR, PADMAVATHI	
ART UNIT	**PAPER NUMBER**
1645	8

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/507,242	Applicant(s) FREDRECKEL ET AL.
	Examiner Padmavathi v Baskar	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/30/01* .

2a)☒ This action is **FINAL**. 2b)☐. This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,8,9 and 23-39* is/are pending in the application.

4a) Of the above claim(s) *3,4 and 8-19* is/are withdrawn from consideration.

5)☒ Claim(s) *1,28 and 29* is/are allowed.

6)☒ Claim(s) *5,6 and 23-27and 30-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,3-6,8,9 and 23-39* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). *8/9/10* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Response to Amendment

1. The amendment filed on 8/30/01 has been entered into the record. Claims 2,7, 20-22 have been canceled. Claims 1 and 5 have been amended. New claims 24-39 have been added. Claims 1, 3-6, 8-9 and 23-39 are pending in the application. Claims 1, 5-6, 23-39 are under examination.

2. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Rejections Withdrawn

3. In view of cancellation of claim 2 and amendment to the claim 1, the rejection under 35 U.S.C. 112, first paragraph (written description, # 9 and 10 of previous office) is withdrawn.

4. In view of amendment to the claims 1 and 5, the rejection under 35 U.S.C. 102 (b) is withdrawn for claims 1 and 5.

Rejections Maintained

5. The rejection of claims 1, 2, 5, 20-23 under 35 U.S.C, 112 first paragraph is maintained as set forth in the previous office action for the new claims 5, 6, 23-26 and 30-39.

The rejection is based on 35 U.S.C 112, first paragraph. The instant claims while being enabling for an isolated or purified nucleic acid consisting of SEQ. ID. NOS: 1, an isolated nucleic acid molecule consisting of OW-216 or OW-221 (SEQ.ID.NOS 3 or 6), a vector comprising or consisting of the nucleic acid molecule of claim 1, a method of preparing CaEss1comprising or consisting of transforming a vector to contain the isolated nucleic acid molecule of claim 1, a method for detecting Candida albicans in a sample comprising or consisting of detecting the presence therein of a nucleic acid molecule of claim 1, method for obtaining an isolated nucleic acid molecule of claim 1 encoding CaESS1 consisting performing

a polymerase chain reaction on a sample suspected to contain CaESS1 using a primer or probe consisting of OW-216 or OW-221 (SEQ.ID.NOS 3 or 6) which specifically hybridize thereto , does not reasonably provide enablement for an isolated or purified nucleic acid consisting essentially of SEQ. ID. N0: 1, and encoding a polypeptide having enzymatic activity of CaEss1, an isolated or purified nucleic acid consisting or consisting essentially of a nucleotide sequence having at least 97% homology to the nucleotide sequence set forth in Figure 1 and encoding a polypeptide having enzymatic activity of CaEss1, an isolated nucleic acid molecule consisting essentially of OW-216 or OW-221 (SEQ.ID.NOS 3 or 6), a vector comprising or consisting of the nucleic acid molecule of claims 24, 25 or 26, a method of preparing CaEss1comprising or consisting of transforming a vector to contain the isolated nucleic acid molecule of claim 24, 25 or 26, a method for detecting Candida albicans in a sample consisting of detecting the presence therein of a nucleic acid molecule of claims 24, 25 or 26, method for obtaining an isolated nucleic acid molecule encoding CaESS1 consisting performing a polymerase chain reaction on a sample suspected to contain CaESS1 using a primer or probe which specifically hybridize thereto.The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant specification provides insufficient support for the claimed invention. Applicants have provided insufficient guidance exactly where to find support in the originally filed specification for the claimed invention as set forth above. Examiner has reviewed the specification and found no support for such language. The specification recites (pages 37-38 and example 3) nucleic acid molecule SEQ.ID.NO 1 and the deduced amino acid sequence SEQ.ID.NO 2, primer or probe consisting of OW-216 or OW-221 (SEQ.ID.NOS 3 or 6), a method for obtaining an isolated nucleic acid molecule encoding CaESS1 consisting performing a polymerase chain reaction on a sample to contain CaESS1 using a primer or probe consisting of OW-216 or OW-221 (SEQ.ID.NOS 3 or 6) However, there is no support that a nucleic acid molecule which encodes a fragment of a polypeptide (i.e., fragment with 97% homology) and a primer or probe which specifically binds to a nucleic acid molecule comprising a nucleotide sequence encoding variant of CaESS1,and a method for obtaining an isolated nucleic acid molecule encoding CaESS1 comprising performing a polymerase chain reaction on a sample to contain CaESS1 using any primer or probe which specifically hybridize thereto Therefore,

applicant is advised to point to the specification where support for this claimed language is drawn and how it conveys the concept of the instant claims .

Scope of enablement requires that the specification teach those in the art to make and use the invention commensurate with the scope of the claim without undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

Applicant has not set forth which nucleic acid molecule encodes a fragment with 97% homology, any probe or primer which hybridizes to the nucleic acid molecule of SEQ.ID.NO 1 and a method for obtaining an isolated nucleic acid molecule encoding a variant of CaESS1 comprising performing a polymerase chain reaction on a sample to contain CaEss1 using any primer or probe. Neither the fragments nor the variants as presently claimed are set forth clearly in the specification.

The instant claims comprising nucleic acid molecule encoding a fragment with 97% homology, any probe or primer which hybridizes to the nucleic acid molecule of SEQ.ID.NO 1 and a method for obtaining an isolated nucleic acid molecule encoding a fragment with 97% CaESS1 comprising performing a polymerase chain reaction on a sample to contain CaEss1 using any primer or probe are not predicted. The specification provides guidance and direction with regard to SEQ.ID.NO 1. 3 and 6. However, there is no guidance or directions on how to make and how to use a polypeptide comprising fragments or variants of CaEss1 with a deletion, of one or more amino acid residues in the amino acid sequence and still retain activity and the ability to generate antibodies. Undue experimentation, without a reasonable expectation of success, is necessary in order to fulfill the claimed invention, an isolated nucleotide molecule comprising a nucleotide sequence encoding CaEss1 having at least 97% homology fragment of SEQ.ID.NO 2 with at least one deletion in the peptide. What changes would have an adverse effect on the function of this peptide is not predictable. It is known in the art that deletions, or modifications of the amino acids of a protein alter the function of the protein. The amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and still retain similar activity/utility requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, the problem of predicting protein structure from mere sequence data of a single protein and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex (Bowie et al. Science, Vol. 247: 1990; p. 1306; p. 1308) and is well outside the realm of routine experimentation.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple modifications of other types and the positions within the protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining similar activity/utility are limited in protein and the result of such modifications is unpredictable based on the instant disclosure.

The specification does not support the broad scope of the claims which encompass a nucleic acid molecule encodes a fragment which can be predictably modified and which regions are critical; what variants, if any, can be made which retain the biological activity of the intact protein; and the specification provide essentially no guidance as to which of the essentially infinite possible choices is likely to be successful. Further, Houghten et al. (Vaccines, 1986,

Edited by Fred Brown: Cold Spring Harbor Laboratory) teach that changes/modifications (addition, substitution, deletion or inversion) of one or more amino acids in a polypeptide will alter antigenic determinants and therefore affect antibody production (p. 21) as well as antibody binding. Houghten et al. also teach that "... combined effects of multiple changes in an antigenic determinant could result in a loss of [immunological] protection." and "a protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies..." (p. 24). Houghten et al. teach that point mutations at one key antigen residue could eliminate the ability of an antibody to recognize this altered antigen (p. 24). It is not always possible to make the derivatives that retain immunodominant regions and immunological activity if the regions have been altered. The specification teaches that specific primer or probes are required to amplify the CaESS1 gene or its use in diagnostic PCR for C.albicans (example 3, specification, pages 37-38). Therefore, any primer or probe would not work to amplify the CaESS1 gene or its use in diagnostic PCR for C.albicans

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed nucleic acid molecule which encodes a fragment of a polypeptide (i.e., fragment with 97% homology), a primer or probe which specifically binds to a nucleic acid molecule comprising a nucleotide sequence encoding any and all variants of CaESS1, and a method for obtaining an isolated nucleic acid molecule encoding CaESS1 comprising performing a polymerase chain reaction on a sample to contain CaESS1 using any primer or probe which specifically hybridize thereto in a manner reasonably correlated with the scope of the claims broadly including any as presently claimed. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made in the protein renders activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. The sequence of some proteins is highly conserved and one skilled in the art would not expect tolerance to any amino acid modification in such proteins. However, even if it were shown that some modifications could be tolerated in the claimed peptides, for the reasons discussed the claims would still expectedly encompass a significant number of inoperative species, which could not be distinguished without undue experimentation. See Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) at 18 USPQ2d 1026-1027 and Ex parte Forman, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986).

Applicant asserts that claims 24 and 26 provide support for 97% homology by providing an algorithm for calculating homology, the nucleic acid molecule encodes a polypeptide having the enzymatic activity of CaEss1 and additionally "consisting essentially of " and functional language recitation provides basic novel characteristics of the invention and cites case law in support (Paper # 7). Examiner disagrees and finds no support for the claimed language in the specification. Indeed the transitional phrase" consisting essentially of " should limit the scope of a claim to the specified materials or steps (MPEP 2111.03). However, presently claimed polypeptide having enzymatic activity and an isolated nucleic acid molecule hybridizing

specifically to the nucleotide sequence set forth in SEQ.ID.NO: 1 have not been shown to have activity so that the use of the claimed invention is enabled. Therefore, this rejection is maintained.

6. The rejection under 35 U.S.C. 102(b) as being anticipated by Accession Number Y 13120 (May 27 1997) and Accession Number AA182274 (January 6 1997) for claim 6 is maintained as set for the in the previous office action for the new claims 5, 6, 27 and 30-31.

Accession Number Y 13120 and Accession Number AA182274 (January 6 1997) disclose a probe consisting essentially of or comprising OW-216 (SEQ.ID.NO 3) and OW-221 (SEQ.ID.NO 6) respectively. Applicant states that the claims now recite, "consisting essentially of " and function and therefore, free of prior art. However, the examiner disagrees with the applicant because the prior art sequence comprises the nucleic acid molecules (i.e., probe) of OW-216 and OW-221. Further, the specification does not provide evidence for functional language (see paragraph # 5 in this office action).

New Rejections Based on Amendment

7. Claims 24 and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Springer et al 1996 (U.S.Patent 5,489,513).

Claims are directed to an isolated or purified nucleic acid molecule consisting essentially of a nucleotide sequence set forth in figure 1, encoding a polypeptide having enzymatic activity of CaEss1 and method of obtaining said nucleic acid molecule.

Springer et al 1996 (U.S.Patent 5,489,513) disclose isolated nucleic acid and method of obtaining said nucleic acid from Candida (see columns 1-4 and column 5, lines 53 through column 6, lines 5). The isolated DNA inherently encodes CaEss1 since it is isolated from Candida and an isolated nucleic acid molecule obtained by PCR. Since the Office does not have the facilities for examining and comparing applicants' product with the product of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed

product and the product of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 27 is rejected as being vague and indefinite for "conditions of high stringency". What are these high stringency conditions?

Status of Claims

9. Claims 1, 28-29 are free of prior art and are in condition for allowance. Claims 33, 34 and 37 would be allowable if amended to dependent from claim 1.

Conclusion

10. This application contains claims 3-4 and 8-19 drawn to an invention nonelected with traverse in Paper No. 6. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Applicant requests the Examiner to reconsider to examine all the claims pending in the application. However, as Examiner pointed out in the previous office action that all these inventions are different structurally, functionally and biochemically. Therefore, it is appropriate to examine the claims 1, 5-6 and 23-39 drawn to polynucleotides in this application.

Applicant states that claim 23 is cancelled and new claim 39 corresponds to the cancelled claim 23 (page 5, first paragraph of applicants amendment 8/30/01). However, claim 23 has not been canceled.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this

Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP ' 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D.

11/14/01

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